DETAILED ACTION

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/680,988, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. There is no disclosure or support for compounds where R =COCOOH, therefore the claims directed compounds containing that limitation will be accorded the filing date of Application No. 10/763,498 of 3/25/2004.

Election/Restrictions

Applicant's election without traverse of Group II, and the species of single compound S36, as encompassed by chemical formula (g) in the reply filed on 11/01/2007 is acknowledged. The restriction is made FINAL.

New claim 44-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 44-46 are directed to compounds, whereas the elected invention is

a method of treatment using the claimed compounds. Because the elected invention is limited to a method for increasing binding of FKBP12.6 to RyR2 in a subject of limiting or preventing a decrease in the level of RyR2-bound FKBP12.6 in a subject, the search is limited to only those methods. Therefore, the search is not co-extensive and extending the search to all methods would be a burden for the Examiner and the claims are not included in the elected invention.

Claims 13, 15, 17-18, 25, 26, 29, 30, 33-35 and 43 are now examined.

Specification

The disclosure is objected to because of the following informalities:

At paragraph 244 on page 63, Applicants state "The inventors' compounds have significantly reduced blocking of hERG (I(Kr)) channels, when compared with JTV-519. As shown in FIGS. 4-7, for example, one of the inventors' compounds, S36, has hERG blocking activity that is approximately 5- to 10-fold lower than the hERG blocking activity of JTV-519. Because the inventors' compounds have weak hERG blocking activity, they are expected to be less toxic than JTV-519."

On the other hand, the description of the figures and the labels on the figures suggest the testing was simply for JTV-519, not the compound S36.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 15, 17, 18, 25, 26, 29, 30, 33-35, and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increases the binding of FKBP12.6 to RyR2 with S36 in a subject, does not reasonably provide enablement for a method for preventing a decrease in the level of RyR2-bound FKBP12.6 in a subject or preventing cardiac conditions generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. Ex Parte Forman, 230 USPQ 546 (Bd Pat. App. & Int. 1986); In re Wands, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 13, 15, 17, 18, 25, 26, 29, 30, 33-35, and 43 are drawn to a method for limiting or preventing a decrease in the level of RyR2-bound FKBP12.6 or treating or preventing a cardiac condition in a subject. Thus, the claimed invention encompasses methods of preventing cardiac conditions.

The specification merely states that S36 prevents cardiac arrhythmias in FKBP12.6+/- mice (see, e.g. Fig 13, page 18, lines 18-23 of the specification). There is

no clear evidence showing that S36 prevents a decrease in the level of RyR2-bound FKBP12.6 in a subject or prevents cardiac conditions other than cardiac arrheythmias. There is not sufficient guidance and/or working examples regarding preventing a decrease in the level of RyR2-bound FKBP12.6 in a subject or preventing cardiac conditions other than cardiac arrheythmias in subjects other than FKBP12.6+/- mice.

The FKBP12.6+/- mice model is fails to provide adequate predictability for all mammals. Examiner cites Xin et al (Oestrogen protects FKBP12.6 null mice from hypertrophy, Nature, v 416 issue 6878, 2002, pp 334-337, specifically pg 336 right column, first full paragraph) which teaches FKBP12.6 knockout mice develop hypertensive cardiac hypertrophy in a sex-specific manner. Further study is required to facilitate investigation of the signaling program triggered by Ca2+ overload and the processes by which sex hormones modulate these effects. Therefore, even in the FKBP12.6 knockout mice model, prior art teaches it results are not predictive for both sexes.

Additionally, Loughrey et al (Cardiovascular Research 76 (2007) 236–246) discloses compounds used in testing the FKBP12.6 binding to RyR2 varied by the animal tested. Loughrey et al taught K201 (JTV-519, the compound S36 is derived from) was ineffective on hearts from FKBP12.6 knockout mice, but effective on rabbits for some of the instantly claimed heart conditions. (see page 245 Discussion 4.5).

Therefore, the FKBP12.6 knockout mouse model is not effective for both sexes, nor is it effective for predictability for all mammals with heart conditions. It is

unpredictable whether S36 would completely prevent arrhythmias and sudden cardiac death in a subject other than FKBP12.6+/- mice.

Additionally, while Applicants state S36 has improved properties of the previously disclosed JTV-519, there is no evidence that would lead one skilled in the art to agree with this assertion. As such, the extensive data provided for testing JTV-519 may or may not be applicable to the derivative, S36.

Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 15, 17, 18, 25, 26, 29, 30, 33-35, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The compounds are defined as the formula “or is any oxidized form thereof.” It is unclear as to where in the molecule such oxidation occurs. Further, if m is 1 or 2, it is unclear if this is considered an “oxidized form thereof.”

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation "wherein the subject … is a candidate for a cardiac condition selected from …" does not adequately define the patient population. For example, everyone would be a "candidate for" heart failure.

Claim 18 recites the limitation "the cardiac condition in the subject" in part (e) of claim 18. There is insufficient antecedent basis for this limitation in the claim where claim 13 only discuses limiting or preventing a decrease in the level of RyR2-bound FKBR12.6 in a s subject.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13, 15, 17, 18, 25, 26, 29, 30, 33-35, and 43 are provisionally rejected on the ground of nonstatutory double patenting over copending Applications No. 11/212,309 (claims 85-106), 11/212,413 (claims 85-106), and 11/506,285 (claims 22-31). This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: All claims are directed to treatment using drugs in the class of compound S36.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin J. Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-R 9-4:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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BP

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